TARGETED GENETICS

February 4, 2005

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane Rm. 1061
Rockville, MD 20852

RE: [Docket Number 2004D-0465] *Draft Guidance for FDA Review Staff and Sponsors: Content and Review of Chemistry, Manufacturing and Control (CMC) Information for Human Gene Therapy Investigational New Drug Applications (INDs)*

Targeted Genetics Corporation (TGC) develops gene-based therapies to prevent or treat acquired, inherited and infectious diseases. We applaud the FDA's efforts in developing the draft guidance document and appreciate the opportunity to provide comments.

General Comment

TGC strongly supports the development of the guidance document. We believe that this document will assist both industry and the agency in setting expectations for CMC content and lead to consistent review practices in this rapidly evolving field.

Specific Comments

Section III.A.2.b.1) Master Cell Bank – *We recommend that ...Product Microbiological characteristics: including sterility, mycoplasma, in vivo and in vitro testing for adventitious viral agents, and replication competent virus (RCV), as appropriate (see section III below).*

Comment: The reference to section III is unclear. Additional guidance with regard to RCV testing was not obvious in the remainder of section III. Please clarify the reference.

Section III.A.2.b.2) Master Viral Bank – *We recommend that you address...Product microbiological characterization including sterility, mycoplasma, in vivo and in vitro testing for adventitious viral agents*

Comment: The standard in vivo and in vitro tests may not be appropriate for viral banks that are, in and of themselves, cytopathic. We recommend that this wording be changed to "*Microbiological characterization including sterility, mycoplasma, in vivo and in vitro testing for adventitious viral agents, as appropriate*". In addition, if specific guidance

2004D-0465 C1

TARGETED GENETICS CORPORATION

1100 Olive Way, Suite 100 Seattle, Washington 98101 Phone 206.623.7612 Fax 206.223.0288

regarding adventitious agents testing of cytopathic viral products is available, please include or reference.

Section III.A.4 Product Manufacturing – Additonal Considerations

Comment: To correct a typographical error, we suggest that the title of this section be changed to "Additional Considerations".

Section III.B Product Manufacturing – Procedures

Comment: The organization of this section, as well as some portions of the testing section, may be a potential area of confusion for reviewers. Clearly distinguish between those sections that are more applicable to cell therapies as opposed to cell-based production of viral products, for example, Section III.B.3. Final Harvest.

Section IV.D Potency

Comment: In vivo or in vitro tests to directly measure biological activity may be difficult or impossible to devise for some gene therapy products. Please address whether suitable surrogate activity assays would be considered.

Section VI.A Stability Testing- "*We believe that a proposed stability protocol should include a measure of product sterility...*"

Comment: Incorporation of USP or 21 CFR 610.12 compliant sterility testing, at multiple time-points, into a stability protocol for final product would require disproportionately large volumes of product, particularly for early-phase materials where product supply may be very limited. Please clarify that "a measure of product sterility" does not necessarily require full USP or 21 CFR 610.12 compliant sterility testing at every stability time-point.

We welcome the opportunity to provide feedback on the *Draft Guidance for FDA Review Staff and Sponsors: Content and Review of Chemistry, Manufacturing and Control (CMC) Information for Human Gene Therapy Investigational New Drug Applications (INDs).* Please contact me if you require clarification or further information regarding our comments.

Sincerely,

Rae Saltzstein

Rae Saltzstein
Director, Quality and Regulatory Affairs
Targeted Genetics Corporation